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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PETERSEN, CLARK D	

ART UNIT	PAPER NUMBER
1657	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,349	DAMGAARD ET AL.	
	Examiner	Art Unit	
	Clark D. Petersen	1657	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 September 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,8,10,12,13,21,30,31 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1-3,8,10,12,13,21,27,30,31,36-38,40,45,51-53,57,60-68,70,4243 and 4849.
Continuation of Disposition of Claims: Claims withdrawn from consideration are 27, 36 -38, 40, 42, 43, 45, 48,49, 51-53, 57, 61-67, AND 70 .

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of Group I, claims 1-3, 8, 10, 12-13, 21, 30-31, and 68 in the reply filed on 17 August 2007 is acknowledged.

Claims 27, 36-38, 40, 42-43, 45, 48-49, 51-53, 57, 60-67, and 70 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Groups, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 17 August 2007.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 8, 10, 12, 13, 21, 30, 31, and 68 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 68 recite "defined by a diffusion barrier and capable of comprising a medium...." While the end of Claim 1 recites "a metabolite diffusion gradient is allowed to be established from the substantially spherical metabolizing particle and throughout the medium...". Claim 2 then recites "wherein the diffusion barrier is constituted by a compartment wall having at least one metabolite permeable opening and the medium". For the instant invention to function, it appears that the medium by definition must be a

diffusion barrier, not that it is a component *in addition to* a diffusion barrier. Furthermore, the limitations of Claim 2 do not limit, but rather alter, the scope of Claim 1 in that the definition of "a medium" has been changed from something outside the scope of a diffusion barrier to something included in a diffusion barrier. Language for claim 1 such as "wherein the diffusion barrier comprises a medium" would make it clearer for one of ordinary skill in the art to reproduce the claimed invention.

The other claims are rejected as depending from Claim 1.

Claim 8 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 8 recites "high-viscosity medium". "High" is a relative term without any reference value. Therefore any medium could be high viscosity depending on the reference point of the reader.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 10, 30-31, and 68 are rejected under 35 U.S.C. 102(b) as being anticipated by Miltenberger et al. (US 4,649,114, issued 10 March 1987).

Miltenberger et al teach a device for culturing mammalian cells. They teach that this device has a diffusion barrier made of silicone rubber or polytetrafluoroethylene that is permeable to oxygen (see Abstract, for example). The barrier is in the form of a tube that is coiled around the chamber, reading on claim 2 (see col. 5 line 50 to col. 6 line 36; see Fig. 2 as examples). This chamber contains an oxygen sensor that measures the amount of oxygen being consumed by the cells in suspension, and which has the capability of adjusting oxygen input in response (see col. 6, lines 37-52, for example). This device is useful for culturing animal cells, which reads on "substantially spherical metabolizing particle" as recited in claim 1 (see Miltenberger et al claim 1, for example). Furthermore Miltenberger et al teach that the device can contain synthetic balls as a support for cell growth, which could read on an individual spherical metabolizing particle; however, because the claims are drawn to a device, the invention of Miltenberger meets the instant claims limitations. Whether one of skill in the art measures one metabolizing particle or many is the user's discretion.

Therefore the teachings of Miltenberger et al are deemed to anticipate instant claims 1, 2, 8, 10, 30-31, and 68.

Claims 1-3, 8, 10, 21, 30, 31, and 68 are rejected under 35 U.S.C. 102(b) as being anticipated by Wodnicka et al (J Biomolecular Screening, 2000).

Wodnicka et al teach a microplate system comprising a luminophore in a gas-permeable matrix; this matrix is attached to the bottom of each microplate well. Cells are allowed to metabolize in the wells, consuming oxygen, which causes a change in the fluorescence properties of the matrix (see Materials and Methods, pp. 142-44, for example). Wodnicka et al teach that with they can only measure cell numbers on the order of thousands to tens of thousands (see Fig. 1, p. 144, for example). However they are measuring single cells, and an embryo, for example, is a spherical metabolizing particle potentially composed of an equal number of cells. Furthermore, the instant application claims a device, regardless of intended use: the device taught by Wodnicka et al meets the structural limitations as instantly claimed.

Therefore the teachings of Wodnicka et al are deemed to anticipate instant claims 1-3, 8, 10, 21, 30, 31, and 68.

Claims 1-3, 8, 10, 12, 13, 21, 30, 31, and 68 are rejected under 35 U.S.C. 102(b) as being anticipated by Houghton et al (Molecular Reproduction and Development, 1996, from Applicant's IDS).

Houghton et al teach a method of measuring single the oxygen gradient of single embryos. They suspend embryos in a medium. They draw a small amount of paraffin saturated with oxygen and an oxygen-detecting fluorophore (pyrene) into a capillary pipette tip with a plunger, followed by drawing the medium containing an embryo. These steps read on a device of claims 13 and 21; the paraffin layer is beneath the embryo/medium, and the plunger changes the size of the compartment defined by the

capillary tip. Different sized embryos can be drawn into different sized capillary tips; this reads on claim 13, reciting an insert which changes the transverse dimensions of the compartment (see Materials and Methods, "Measurement of Oxygen Consumption, pp. 477-478, for example).

Therefore the teachings of Houghton et al are deemed to anticipate instant claims 1-3, 8, 10, 12, 13, 21, 30, 31, and 68.

Claims 1-3, 8, 10, 30, 31, and 68 are rejected under 35 U.S.C. 102(b) as being anticipated by Trimarchi et al (Biology of Reproduction, 2000).

Trimarchi et al teach a method of measuring oxygen gradients around developing mouse embryos. The embryos are arranged in open Petri dishes, reading on instant claims 2 and 3; they are bathed in HKSOM, an aqueous medium, reading on instant claim 8. A microelectrode is brought within a few microns of each embryo and the oxygen gradient is measured (see Materials and Methods, pp. 1867-1868, for example).

Therefore the teachings of Trimarchi et al are deemed to anticipate instant claims 1-3, 8, 10, 30, 31, and 68.

Claims 1-3, 8, 10, 21, 30, 31, and 68 are rejected under 35 U.S.C. 102(a) as being anticipated by EP 1,134,583 A1 (no author listed), published 19 September 2001, from Applicant's IDS of 10 Nov 2005). This application teaches a method of measuring metabolic gas diffusion from a microorganism (plant embryo) by placing it in a closed container and submerging the seeds in water (medium). The container inner wall has

attached to it a gas permeable membrane that contains a gas-reactive compound that fluoresces when bound to oxygen and illuminated with a laser (see p. 5, lines 3-33, for example). The medium is water, which is higher viscosity than air, for example.

Therefore the teachings of EP 1,134,583 A1 are deemed to anticipate instant claims 1-3, 8, 10, 21, 30, 31, and 68.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-3, 8, 10, 21, 30, 31, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Miltenberger et al (US 4,649,114).

The teachings of Miltenberger et al are discussed above and applied as before.

Additionally Miltenberger et al suggest that the oxygen diffusion barrier need not take the form of a tube. They suggest that the membrane can have any suitable size or geometric shape, and that it can comprise only a portion of a chamber surface (see col. 4, lines 3-19, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to fashion a chamber floor or portion of a chamber wall from a gas permeable material because Miltenberger et al suggest that a gas permeable diffusion barrier of any surface or portion of a surface is suitable in their invention.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to fashion a chamber for growing and monitoring spherical particles that included an oxygen-permeable floor or portion of any other surface.

Claims 1-3, 8, 10, 12, 13, 21, 30, 31, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schwarz et al (US 5,763,279, issued 9 June 1998) in view of Miltenberger et al (US 4,649,114).

Schwarz et al teach a bioreactor. The bioreactor has walls that are manufactured partially or wholly from an oxygen-permeable material (see col. 2, lines 48-57, for example). The device contains a slot for positioning an insert that can divide the chamber into two parts, reading on instant claim 12 (see col. 7, lines 15-35, for example). Additionally the chamber can be constructed of two tubes, one within the other, that can slide back and forth so that the volume of the chamber between the two tubes can be adjusted. The vessel has ports for inserting instruments into the variable-volume chamber (see col. 8, lines 3-16, for example).

Schwarz et al do not expressly teach that oxygen should be monitored by an oxygen sensor.

Miltenberger et al teach that in a chamber with oxygen diffusion surfaces one can actively pump oxygen into the chamber and monitor oxygen levels with an oxygen sensor to ensure uniform, abundant oxygen levels in the cell growth medium (see col. 6, lines 37-52, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to provide an oxygen-permeable chamber whose volume is adjustable by means of inserts or adjustable bottom because Schwarz et al teach a chamber with oxygen-permeable walls in which barriers can be inserted or the bottom adjusted, and Miltenberger et al teach that a chamber with oxygen-permeable surfaces can have oxygen actively provided to it, and that the oxygen levels can be monitored and adjusted by means of an oxygen sensor.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to provide a chamber with an oxygen sensor which had gas permeable surfaces and means for adjusting the volume of the chamber.

Claims 1-3, 8, 10, 21, 30, 31, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barbera-Guillem et al (US PGPub 2002/0072113 A1, published 13 June 2002) in view of Jung et al (Anal Chem, Sept 1999).

Barbera-Guillem et al teach a chamber for monitoring cells. The chamber comprises a gas permeable membrane made of a high-viscosity material such as silicone. The chamber also contains an access port for inserting a needle (see para [0026], for example). They teach that their system is useful for monitoring cell parameters over an extended period of time (see paras [0004]-[0010], for example).

Barbera-Guillem et al do not expressly teach the measurement of oxygen diffusion from a cell in the chamber.

Jung et al teach a method of measuring oxygen diffusion from a single pancreatic islet. They use a platinum wire inserted into a syringe and place it near a cell in a dish. They then can measure the oxygen diffusion from the cell in response to providing different concentrations of glucose (see Experimental Section, pp. 3644-3645, for example). They teach that measurement of single cells or single units of tissue can be important in understanding phenomena in diabetes for example (see Introduction, pp. 3642-3643, for example).

A person of ordinary skill in the art at the time the invention was made would have been motivated to measure oxygen diffusion from a single cell particle in a device with a gas permeable chamber because Barbera-Guillem et al teach that cells can be monitored over longer periods of time in a chamber with gas permeable surface and a port for insertion of a needle, and Jung et al teach that the basis of certain diseases can be understood by monitoring a cell's oxygen consumption over a period of time by means of a device comprising a platinum wire inserted in a needle.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to provide a chamber with oxygen-permeable surface and means for inserting a needle containing an oxygen electrode to monitor oxygen at a single cell or single group of cells.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Clark D. Petersen whose telephone number is (571)272-5358. The examiner can normally be reached on M-F 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached on (571)272-0925. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

CDP 10/18/2007

/Jon P Weber/
Jon P Weber
Supervisory Patent Examiner 1657